# Asthma among adult patients presenting with dyspnea to the emergency department: An observational study

Kuan, Win Sen; Craig, Simon; Kelly, Anne Maree; Keijzers, Gerben; Klim, Sharon; Graham, Colin A.; Jones, Peter; Holdgate, Anna; Lawoko, Charles; Laribi, Said

*Published in:*
Clinical Respiratory Journal

*DOI:*
10.1111/crj.12782

**Title of Manuscript**: Asthma among adult patients presenting with dyspnea to the emergency department: an observational study

**Author List**: Win Sen Kuan[1,2] MBBS, MRCSEd(A&E), MCI, FAMS; Simon Craig[3,4,5] MBBS, FACEM, MHPE; Anne-Maree Kelly[6,7] MD, FACEM, FCCP; Gerben Keijzers[8,9,10] MSc (Biomed Health Sci), MBBS, FACEM, PhD; Sharon Klim[6] BN; Colin A Graham[11] MD, MPH, FRCP, FRCS, FCCP, FCEM, FHKCEM, FHKAM; Peter Jones[12,13] FACEM, BSc, EBHC (Oxon); Anna Holdgate[14,15] MBBS, FACEM, MMed; Charles Lawoko[16] PhD, MA; Said Laribi[17,18] , PhD

**Author Affiliations**:

[1] Emergency Medicine Department, National University Hospital, National University Health System, Singapore

[2] Department of Surgery, Yong Loo Lin School of Medicine, National University of Singapore

[3] Emergency Department, Monash Medical Centre, Clayton, Australia

[4] School of Clinical Sciences, Monash University, Clayton, Australia

[5] Murdoch Children's Research Institute, Parkville, Australia

[6] Joseph Epstein Centre for Emergency Medicine Research @ Western Health, Sunshine Australia

[7] Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Parkville, Australia

[8] Department of Emergency Medicine, Gold Coast University Hospital, Gold Coast, Australia

[9] School of Medicine, Bond University, Gold Coast, Australia

[10] School of Medicine, Griffith University, Gold Coast, Australia

[11] Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong SAR

[12] Department of Emergency Medicine, Auckland City Hospital, Auckland, New Zealand

[13] Department of Surgery, University of Auckland, Auckland, New Zealand

[14] Department of Emergency Medicine, Liverpool Hospital, Sydney, Australia

[15] University of New South Wales (Southwest Clinical School), Sydney, Australia

[16] Industry Doctoral Training Centre, ATN Universities, Melbourne, Australia

[17] Francois Rabelais University, School of Medicine, Tours, France

[18] Tours University Hospital, Emergency Medicine Department, Tours, France

**Corresponding Author:**

Dr. Win Sen Kuan

Emergency Medicine Department, National University Hospital, 5 Lower Kent Ridge Road, Singapore 119074

E-mail: win_sen_kuan@nuhs.edu.sg

Tel: +65 67722452

Fax: +65 67758551

**Running Title:** Asthma in Asia Pacific Emergency Departments

**Prior Presentation:** Presented at the Australasian College for Emergency Medicine Annual Scientific Meeting on 23 November 2015 in Brisbane, Queensland, Australia

**Funding Source:** This work was supported by a grant from the Queensland Emergency Medicine Research Foundation; grant number EMPJ-108R21-2014

**Author Statement:**

SC, AMK, GK, CAG, PJ, AH and SL came up with the study concept and design. WSK, SC, GK, SK, CAG and PJ collected the data. WSK, SC, AMK, GK and PJ were involved in the analysis and interpretation of the data. WSK, SC and AMK drafted the manuscript. WSK, SC, AMK, GK, CAG, PJ, AH and SL critically revised the manuscript for important intellectual content. WSK, AMK and CL contributed statistical expertise. AMK, GK, SK and CAG obtained funding. SK provided administrative and technical support. AMK, GK, CAG and SL provided study supervision.

**Disclosures:** All authors have no potential conflicts to disclose.

**Abstract**

*Introduction*: Shortness of breath is a common presenting symptom to the emergency department (ED) that can arise from a myriad of possible diagnoses. Asthma is one of the major causes.

*Objective*: To describe the demographic features, clinical characteristics, management and outcomes of adults with an emergency department (ED) diagnosis of asthma who presented to an ED in the Asia Pacific region with a principal symptom of dyspnea.

*Methods*: Planned sub-study of patients with an ED diagnosis of asthma identified in the Asia, Australia and New Zealand Dyspnoea in Emergency Departments (AANZDEM) study. AANZDEM was a prospective cohort study conducted in 46 EDs in Australia, New Zealand, Singapore, Hong Kong and Malaysia over three 72-hour periods in May, August and October 2014. Primary outcomes were patient epidemiology, clinical features, treatment and outcomes (hospital length of stay (LOS) and mortality).

*Results*: Of the 3,044 patients with dyspnea, 387 (12.7%) had an ED diagnosis of asthma. The median age was 45 years, 60.1% were female, 16.1% were active or recent smokers, and 30.4% arrived by ambulance. Inhaled bronchodilator therapy was initiated in 88.1% of patients and 66.9% received both inhaled bronchodilators and systemic corticosteroids. After treatment in the ED, 65.4% were discharged. No death was reported.

*Conclusion*: Asthma is common among patients presenting with a principal symptom of dyspnea in the ED of the Asia Pacific region. There was suboptimal adherence to international guidelines on investigations and treatments of acute asthma exacerbations presenting an opportunity to improve efficiency of care.

*Keywords*: Asthma; epidemiology; emergency services, hospital; dyspnea

## Introduction

Shortness of breath is a common presenting symptom to the emergency department (ED) that can arise from a myriad of possible diagnoses.[1] Major etiological groups are cardiac and respiratory disease; among the latter asthma is one of the major causes.

The World Health Organization estimates that over 235 million people suffer from asthma globally. There is large variability in the prevalence of asthma among countries worldwide; the highest being over 20% reported in Australia.[3,4] Morbidity, mortality and the number of disability-adjusted life years lost due to asthma are substantial, particularly in lower income nations.[5,6] The incidence of asthma exacerbations varies with seasons, environmental conditions and air pollutants.[7-9] Frequent attendances to the ED by asthmatic patients have been associated with higher mortality.[10,11]

National and international guidelines recommend a number of treatments to optimize outcomes.[12-14] These include inhaled bronchodilators, systemic corticosteroids and targeted oxygen therapy. There is limited information on the epidemiology of asthma in the Asia Pacific region and about compliance with guideline recommended therapies.

The objective of this planned sub-study is to describe the demographics, clinical characteristics, treatment and patient outcomes of the cohort of patients who attended the ED in the Asia Pacific region with a primary symptom of dyspnea, and have a subsequent ED diagnosis of asthma.

## Materials and Methods

The methodology of this study has been published previously.[15] Briefly, the Asia, Australia and New Zealand Dyspnoea in Emergency Departments (AANZDEM) study is a prospective, descriptive cohort study conducted at three time points in 46 EDs in Australia,

New Zealand, Singapore, Hong Kong and Malaysia of consecutive adult patients presenting to the ED with dyspnea as a main symptom. Data were collected over three 72-hour periods (13-16 May 2014, 12-15 August 2014 and 14-17 October 2014), which corresponded to the seasons of autumn, winter and spring in Australasia. Variables collected included demographics, comorbidities, mode of arrival, usual medications, pre-hospital treatment, initial assessment, ED investigations, treatment in the ED, ED diagnosis, disposition from the ED, in-hospital outcome and final hospital diagnosis.

This planned sub-study includes patients in the AANZDEM study with an ED diagnosis of asthma. The primary outcomes of interest are the epidemiology, investigations ordered, treatments given and overall outcomes of these patients. Secondary outcomes consist of geographical variations of the primary outcomes and adherence to international guidelines on asthma management. Guidelines for the initial assessment of severity of acute asthma exacerbations in adults include evaluation of symptoms, vital signs, measurement of peak expiratory flow rate, and indications for blood gas and chest radiograph. Guidelines for treatment of acute asthma encompasses indications for the provision of supplemental oxygen, steroid therapy, beta2-agonist bronchodilators, ipratropium bromide, other forms of adjunctive therapy such as intravenous magnesium sulfate and prescription of antibiotics.

Analysis was largely by descriptive statistics. Comparisons of proportions and measures of associations were done using the Chi-square or Fisher's exact test, where appropriate. Non-parametric data were compared using the Mann-Whitney *U* test. Data analyses were performed with IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY) and Analyse-it for Microsoft Excel, Version 2.20 (Analyse-it Software, Ltd., Leeds, UK). This analysis used data which was collected for studies about patients presenting to ED with dyspnea. Hence, a priori sample size calculations were not necessary. There may have been situations where the same patient presented more than once and these were not de-

duplicated. However, given the large sample sizes of the groups, this matter would be expected to have minimal impact on the results presented or the outcomes of the analyses performed. Reporting of results complies with the STROBE guidelines.[16] It should be noted that only specific statistical tests (and hence P-values) were performed and reported, in order to avoid inflating Type 1 error. Human research ethics approvals were obtained for all sites according to local requirements. Most jurisdictions did not require patient consent for data collection. Some sites in Queensland required patient consent so that part of the data is not consecutive.

## Results

### Characteristics of Study Subjects

Forty-six EDs contributed data on 3,044 patients with dyspnea as a presenting symptom. Thirty-three sites were in Australia, 4 in New Zealand, 4 in Hong Kong, 3 in Singapore and 2 in Malaysia. In 2014, the study sites had a combined annual ED census of 2,886,178 patients. (See Acknowledgements for full list)

Three hundred eighty-seven patients had an ED diagnosis of asthma (12.7%; 95% confidence interval (CI) 11.6 to 14.0%). Asthma cases contributed to 0.64% (387/60,059) of all ED attendances in the study periods. There was a higher incidence of asthma exacerbations among dyspneic patients in the EDs of Asian countries (171/1,086, 15.7%; 95% CI 13.7 to 18.1%) compared to Australia and New Zealand (216/1,958, 11.0%; 95% CI 9.7 to 12.5%).

Over 75% of patients were younger than 60 years (Table 1). There was a greater proportion of female patients with asthma in the EDs of Australia and New Zealand (ANZ) compared to South East Asia (SEA) (65.3 vs. 53.2%). The overall smoking prevalence was

16.1%, again a much higher preponderance in ANZ compared to SEA (22.1 vs. 8.8%). Over 90% of patients were previously diagnosed with asthma and 6% had a concomitant history of chronic obstructive pulmonary disease. Just under one-third (30.4%) arrived to the ED by ambulance; many more in ANZ than in SEA (37.3 vs. 21.7%).

**Medications**

Common pre-existing prescribed asthma medications are also described in Table 1 and included: inhaled beta-sympathomimetics (74.9%), inhaled corticosteroids (46.0%), inhaled anticholinergics (14.7%) and oral corticosteroids (13.5%). There were more patients who were on inhaled anticholinergics (16.4 vs. 8.2%), inhaled corticosteroids (52.3 vs. 38.0%), and oral corticosteroids (17.4 vs. 8.8%) in ANZ versus SEA.

**Clinical features**

Clinical features including physical examination findings are shown in Table 2. The majority of patients experienced between 1 and 4 days of shortness of breath before presenting to the ED. A small proportion (6.1%) had documented fever. There were 18.7% who had more severe symptoms, at best being able to only speak in phrases. Over 10% experienced severe tachypnea (respiratory rate ≥30 breaths per minute). More than 80% were found to have wheeze or rhonchi during examination.

**Investigations**

Chest radiographs were obtained in 70.4% of patients and 23.5% had blood gas analysis (Table 2).

**Treatment**

More than 70% did not receive any form of initial oxygen therapy in the ED (Table 3). Only 1 patient received non-invasive ventilation and none required endotracheal intubation. Over 88% received inhaled bronchodilator therapy and a lower proportion (69.7%) received systemic corticosteroids. Two-thirds of patients received both inhaled bronchodilators and systemic corticosteroids. More patients were prescribed antibiotics for their asthma exacerbation in ANZ compared to SEA (30.5 vs. 14.0%).

**Outcomes**

Almost two-thirds were discharged from the ED, including those who were managed in an ED observation unit (Table 3). Eleven (2.8%) patients required admission to the intensive care unit and there were no deaths reported in our cohort. Among those who required admission to the hospital wards, the median length of stay was 4 days (interquartile range 3-6 days). Of those patients admitted to hospital with asthma, asthma was confirmed as the final primary diagnosis in 84% with lower respiratory tract infection (9%) and chronic obstructive pulmonary disease (7%) being the alternative primary diagnoses.

## Discussion

Our study shows that asthma is a relatively common diagnosis encountered in adult patients presenting with dyspnea to the ED in the Asia Pacific region, accounting for a higher proportion of cases in SEA compared to ANZ. We also found that compliance with guideline recommended investigations and treatments were suboptimal, from high utilization of chest radiographs and blood gas analyses, and increased proportion of inhaled ipratropium bromide administration and prescription of antibiotics, respectively. The results of this study could be a useful baseline reference for which future ED studies on asthma in the region could be

based upon after education and promulgation of management guidelines and recommendations.[12-14]

Over the last 25 years, the epidemiology of asthma exacerbations has changed to one of decline in hospitalization rates postulated to be due to increased use of asthma control medications, lower tendency for clinicians to admit patients and administrative incentives in certain countries to reduce hospital admission.[17] However, the disposition of patients presenting to the ED in our study is somewhat dissimilar to those previously published in North America.[18] The proportion of patients admitted to the hospital ward was much higher in our cohort (31.5% vs. 7.0%).[18] We surmise that the reasons could include higher severity of asthma exacerbations in the region. Our rationale for this is the high proportion of patients who arrived to the ED by ambulance (30.4%) (Table 1); the frequency of signs suggestive of severe disease [difficulty speaking (18.7%) and high respiratory rate (10.9%)] (Table 2); and the prolonged median length of stay of 4 days for admitted patients (Table 3). Another explanation could be how the different populations use the ED. In Australasia there is ready access to primary health care that is affordable. Patients with less severe disease may have sought care there rather than the ED.

The Global Initiative for Asthma[12], Australian Asthma Handbook[13], and British Thoracic Society[14] provide guidelines for the management of asthma in acute care settings such as the ED. The guidelines include assessment, treatment, review of response and discharge planning of asthma exacerbations. Supplemental controlled low flow oxygen therapy is recommended to maintain saturation at 93-95%. The majority of patients in our cohort (70.8%) did not receive any supplemental oxygen and only a small proportion received untitrated supplemental oxygen via face mask (11.9%) and non-rebreather mask (1.8%). We were unable to determine whether the target oxygen saturations were met due to lack of data collected after initiation of oxygen therapy.

Inhaled short-acting beta2-agonists and systemic corticosteroids are both mainstays of management for acute asthma exacerbations. Furthermore, there is strong evidence that systemic corticosteroids hasten the resolution of exacerbations and prevent relapses.[19] In spite of this, a less than optimal 66.8% of patients received both forms of therapy in our study, suggesting room for improvement in efficiency of asthma care with regard to compliance to guidelines.

Slightly over half (55.8%) of patients with asthma exacerbations in this study received inhaled anticholinergic therapy during their ED visit. Current guidelines by the Expert Panel of the National Asthma Education and Prevention Program recommend inhaled ipratropium be used for patients with severe exacerbations in the ED.[20] We were unable to collect on structured severity assessment as different sites used different methods but if the admission rate of approximately 30% is taken as a proxy for more severe disease, it would appear that there was a disproportionately higher use of inhaled anticholinergics for the milder forms of asthma exacerbations in our cohort.

Chest radiographs and blood gas measurements are not routinely recommended for adults with asthma exacerbations unless patients are not responding to initial therapy or are deteriorating.[12,14] In our study, 70.4% of patients had a chest radiograph done. Previous studies reported only about 2% abnormal findings from chest radiographs among acute asthmatics in the ED.[21,22] Similarly, 23.5% of patients had blood gas analysis but only 2.8% were eventually admitted to the intensive care unit. Reasons for the overuse of chest radiographs is unclear but may represent habit or a lack of awareness of the evidence and guideline recommendations. We reported data on blood gas analysis but did not differentiate between arterial and venous analyses. It is possible that clinicians used a venous blood gas analysis to screen for hypercarbia in patients where there was clinical concern of severe disease.[23]

Many factors can trigger an asthma exacerbation. Most respiratory infections that trigger the exacerbation are viral in origin. Hence, routine use of empiric antibiotic therapy is not recommended.[12,14, 24,25] Despite this, there was a high proportion (23.2%) of antibiotic usage in our study even though symptoms and signs of bacterial infection were lacking. Inappropriate use of antibiotics has driven the rapid increase in antibiotic resistance, and compounded by the dearth of new antibiotics in the pipeline, a post-antibiotic era is looming.[26]

While lack of knowledge may be a contributor to failures to comply with guideline-recommended investigation and treatment, it is more likely that the major reason is human error with contributing factors such as time constraints in ED, distraction and competing patient priorities as several patients are being processed by a doctor at any given time, imperfect memory, and cognitive overload. High staff turnover makes it difficult to ensure all staff are educated in clinical rationale for investigation and treatment, and guideline recommendations for all conditions encountered in the ED. One approach suggested to address deficits in care provided includes the introduction of an asthma proforma or checklist. An alternative approach would be the use of clinical informatics systems such as computer-assisted decision support, which has been proven to improve patient safety and has been recommended by the US Agency for Healthcare Research and Quality.[27] This can range from simple reminder systems to monitor-based color-coded guideline compliance visual alerts.

Our study has several limitations that should be considered when interpreting our results. First, the results may not be generalizable to other regions outside of South East Asia and Australasia as health care access and affordability, particularly to the ED, may differ. Second, asthma as a diagnosis was based on the treating ED clinician's judgment. Although potentially subject to error in part related to incomplete information and investigations, this represents the 'real world' practice in EDs. Determination of patients who required guideline

recommendations in the management of their acute asthma exacerbations were not individually detailed, which could have blunted the ascertainment of compliance to guidelines. Third, the severities of asthma exacerbations were not explicitly measured. Helpful information on asthma phenotype through information on history of chronicity, differentiation between short- and long-acting bronchodilator use, utilization of combination treatment of inhaled corticosteroids and long-acting bronchodilators, and frequency of exacerbations were not collected. It would have been useful to have had information on other investigations and treatment modalities, such as peak flow measurements or spirometry but these are inconsistently performed in ED.[28] We did not have data on intravenous administration of magnesium sulfate to better assess compliance to international guidelines for patients with severe asthma.

## Conclusions

In conclusion, this study on patients with asthma provides a unique understanding of regional variation in demographics, investigations and treatment in a cohort of patients from EDs in the Asia Pacific region. There was seemingly suboptimal adherence to international guidelines on investigations and treatments, which alerts us to an opportunity to improve efficiency of care.

**Acknowledgments:**

**AANZDEM Steering Committee**

Anne-Maree Kelly (Chair), Gerben Keijzers (Vice-chair and Queensland), Simon Craig (Victoria), Colin Graham (Hong Kong), Anna Holdgate (NSW), Peter Jones (New Zealand), Win Sen Kuan (Singapore), Said Laribi (France).

**AANZDEM Study Group** (includes all hospitals that expressed interest in participation, identified a project lead and had ethics approval)

Richard McNulty (Blacktown and Mt Druitt Hospitals NSW), David Lord Cowell (Dubbo Hospital NSW), Anna Holdgate and Nitin Jain (Liverpool Hospital NSW), Tracey de Villecourt (Nepean Hospital NSW), Kendall Lee (Port Macquarie Hospital NSW), Dane Chalkley (Royal Prince Alfred Hospital NSW), Lydia Lozzi (Royal North Shore Hospital NSW), Stephen Asha (St George Hospital NSW), Martin Duffy (St Vincent's Hospital Sydney NSW), Gina Watkins (Sutherland Hospital NSW), David Rosengren (Greenslopes Private Hospital QLD), Jae Thone (Gold Coast Hospital QLD), Shane Martin (Ipswich Hospital QLD), Ulrich Orda (Mt Isa Hospital QLD), Ogilvie Thom (Nambour Hospital QLD), Frances Kinnear and Michael Watson (Prince Charles Hospital QLD), Rob Eley (Princess Alexandra Hospital QLD), Alison Ryan (Queen Elizabeth II Jubilee Hospital QLD), Douglas Morel (Redcliffe Hospital QLD), Jeremy Furyk (Townsville Hospital QLD), Richard Smith (Bendigo Hospital VIC), Michelle Grummisch (Box Hill Hospital VIC), Robert Meek (Dandenong Hospital VIC), Pamela Rosengarten (Frankston Hospital VIC), Barry Chan and Helen Haythorne (Knox Private Hospital VIC), Peter Archer (Maroondah Hospital VIC), Simon Craig and Kathryn Wilson (Monash Medical Centre VIC), Jonathan Knott (Royal Melbourne Hospital VIC), Peter Ritchie (Sunshine Hospital VIC), Michael Bryant (Footscray Hospital VIC), Stephen MacDonald (Armadale Hospital WA), Mlungisi Mahlangu (Peel

Health WA), Peter Jones (Auckland City Hospital New Zealand), Michael Scott (Hutt Valley Hospital New Zealand), Thomas Cheri (Palmerston North Hospital New Zealand), Mai Nguyen (Wellington Regional Hospital New Zealand), Colin Graham and Melvin Chor (Prince of Wales Hospital Hong Kong), Chi Pang Wong and Tai Wai Wong (Pamela Youde Nethersole Eastern Hospital Hong Kong), Ling-Pong Leung (Queen Mary Hospital Hong Kong), Chan Ka Man (Tuen Mun Hospital Hong Kong), Ismail Mohd Saiboon (Hospital Universiti Kebangsaan Malaysia, Nik Hisamuddin Rahman (Hospital Universiti Sains Malaysia), Wee Yee Lee (Changi General Hospital Singapore), Francis Chun Yue Lee and Shaun Goh (Khoo Teck Puat Hospital Singapore), Win Sen Kuan (National University Hospital Singapore), Sharon Klim, Kerrie Russell & Anne-Maree Kelly (AANZDEM coordinating centre), Gerben Keijzers, & Said Laribi (steering committee) and Charles Lawoko (ATN universities, statistician)

## References


1. Parshall MB, Schwartzstein RM, Adams L, et al. An official American Thoracic Society statement: update on the mechanisms, assessment, and management of dyspnea. Am J Resp Crit Care Med. 2012;185:435-452.
2. World Health Organisation. Fact sheets, Asthma. Available at: http://www.who.int/mediacentre/factsheets/fs307/en/. Accessed May 14, 2017.
3. Akinbami LJ, Moorman JE, Bailey C, et al. Trends in asthma prevalence, health care use, and mortality in the United States, 2001-2010. NCHS Data Brief. 2012;94:1-8.
4. To T, Stanojevic S, Moores G, et al. Global asthma prevalence in adults: findings from the cross-sectional world health survey. BMC Public Health. 2012;12:204.
5. Bousquet J, Bousquet PJ, Godard P, Daures JP. The public health implications of asthma. Bull World Health Organ. 2005;83:548-554.
6. Thompson PJ, Salvi S, Lin J, et al. Insights, attitudes and perceptions about asthma and its treatment: findings from a multinational survey of patients from 8 Asia-Pacific countries and Hong Kong. Respirology. 2013;18:957-967.
7. Larsen K, Zhu J, Feldman LY, et al. The Annual September Peak in Asthma Exacerbation Rates. Still a Reality? Ann Am Thorac Soc. 2016;13:231-239.
8. Fan J, Li S, Fan C, Bai Z, Yang K. The impact of PM2.5 on asthma emergency department visits: a systematic review and meta-analysis. Environ Sci Pollut Res Int. 2016;23:843-850.
9. Haikerwal A, Akram M, Sim MR, Meyer M, Abramson MJ, Dennekamp M. Fine particulate matter (PM2.5) exposure during a prolonged wildfire period and emergency department visits for asthma. Respirology. 2016;21:88-94.

10. To T, Zhu J, Williams DP, et al. Frequency of health service use in the year prior to asthma death. J Asthma. 2016;53:505-509.
11. Ahmed AE, Al-Jahdali H, Al-Harbi A, et al. Factors associated with poor asthma control among asthmatic patient visiting emergency department. Clin Respir J. 2014;8:431-436.
12. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2016. Available at: ginasthma.org. Accessed May 14, 2017.
13. Australian Asthma Handbook 2016. Available at: https://www.asthmahandbook.org.au/acute-asthma/clinical. Accessed July 12, 2017.
14. BTS/SIGN British guideline on the management of asthma. Available at: https://www.brit-thoracic.org.uk/standards-of-care/guidelines/btssign-british-guideline-on-the-management-of-asthma/. Accessed September 5, 2017.
15. Kelly AM, Keijzers G, Klim S, et al. Asia, Australia and New Zealand Dyspnoea in Emergency Departments (AANZDEM) study: Rationale, design and analysis. Emerg Med Australas. 2015;27:187-191.
16. STROBE statement. Strengthening the reporting of observational studies in epidemiology. Available at: http://www.strobe-statement.org/. Accessed May 14, 2017.
17. Johnston NW, Sears MR. Asthma exacerbations. 1: epidemiology. Thorax. 2006;61:722-728.
18. Hasegawa K, Sullivan AF, Tovar Hirashima E, et al. A multicenter observational study of US adults with acute asthma: who are the frequent users of the emergency department? J Allergy Clin Immunol Pract. 2014;2:733-740.

19. Edmonds ML, Milan SJ, Camargo CA Jr., Pollack CV, Rowe BH. Early use of inhaled corticosteroids in the emergency department treatment of acute asthma. Cochrane Database Syst Rev. 2012;12:CD002308.

20. National Asthma Education and Prevention Program: Expert Panel Report III: Guidelines for the diagnosis and management of asthma. Available at: https://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines/full-report. Accessed May 14, 2017.

21. Findley LJ, Sahn SA. The value of chest roentgenograms in acute asthma in adults. Chest.1981;80:535-536.

22. Zieverink SE, Harper AP, Holden RW, Klatte EC, Brittain H. Emergency room radiography of asthma: an efficacy study. Radiology. 1982;145:27-29.

23. Kelly AM, Kerr D, Middleton P. Validation of venous $pCO_2$ to screen for arterial hypercarbia in patients with chronic obstructive airways disease. J Emerg Med. 2005;28:377-379.

24. Johnston SL, Szigeti M, Cross M, et al. Azithromycin for Acute Exacerbations of Asthma: The AZALEA Randomized Clinical Trial. JAMA Intern Med. 2016;176:1630-1637.

25. Lazarus SC. Clinical practice. Emergency treatment of asthma. N Engl J Med. 2010;363:755-764.

26. Silver LL. Challenges of antibacterial discovery. Clin Microbiol Rev. 2011;24:71-109.

27. Ortiz E, Meyer G, Burstin H. Clinical Informatics and Patient Safety at the Agency for Healthcare Research and Quality. J Am Med Inform Assoc. 2002;9:s2–s7.

28. Nathan RA, Meltzer EO, Blaiss MS, Murphy KR, Doherty DE, Stoloff SW. Comparison of the Asthma in America and Asthma Insight and Management surveys: did asthma burden and care improve in the United States between 1998 and 2009? Allergy Asthma Proc. 2012;33:65-76.

Table 1. Patient Characteristics

| Variable | Total population (N=387) | Missing data | ANZ (n=216) | SEA (n=171) |
|---|---|---|---|---|
| Age (years), median (IQR) | 45 (31-60) | 1 (SEA) | 44 (31-59) | 48 (29-60) |
| Age group, No. (%; 95% CI) | | | | |
| 18-40 years | 159 (41.1; 36.2 to 46.2) | 1 (SEA) | 91 (42.1; 35.5 to 49.0) | 68 (39.8; 32.5 to 47.6) |
| 41-60 years | 136 (35.1; 30.4 to 40.2) | | 76 (35.2; 28.9 to 42.0) | 60 (35.1; 28.1 to 42.8) |
| 61-75 years | 55 (14.2; 11.0 to 18.2) | | 31 (14.4; 10.1 to 19.9) | 24 (14.0; 9.4 to 20.4) |
| >75 years | 36 (9.3; 6.7 to 12.8) | | 18 (8.3; 5.2 to 13.1) | 18 (10.5; 6.5 to 16.4) |
| Female gender, No. (%; 95% CI) | 232 (60.1; 55.0 to 65.0) | 1 (SEA) | 141 (65.3; 58.5 to 71.5) | 91 (53.5; 45.8 to 61.2) |
| Co-morbidities, No. (%; 95% CI) | | | | |
| Previous diagnosis asthma | 351 (90.9; 87.5 to 93.5) | 1 (ANZ) | 195 (90.7; 85.8 to 94.1) | 156 (91.2; 85.7 to 94.8) |
| Active or recent smoker | 62 (16.1; 12.7 to 20.3) | 3 (ANZ) | 47 (22.1; 16.8 to 28.4) | 15 (8.8; 5.2 to 14.3) |
| Chronic obstructive pulmonary disease | 23 (6.0; 3.9 to 9.0) | 3 (ANZ) | 16 (7.5; 4.5 to 12.1) | 7 (4.1; 1.8 to 8.6) |
| Cardiac failure | 8 (2.1; 1.0 to 4.2) | 3 (ANZ) | 5 (2.3; 0.9 to 5.7) | 3 (1.8; 0.5 to 5.4) |
| Diabetes mellitus | 46 (12.0; 9.0 to 15.8) | 3 (ANZ) | 27 (12.7; 8.7 to 18.1) | 19 (11.1; 6.7 to 17.0) |
| Dyslipidemia | 61 (15.9; 12.5 to 20.0) | 3 (ANZ) | 29 (13.6; 9.5 to 19.1) | 32 (18.7; 13.3 to 25.5) |

| | | | | |
|---|---|---|---|---|
| Hypertension | 92 (24.0; 19.8 to 28.6) | 3 (ANZ) | 48 (22.5; 17.2 to 28.9) | 44 (25.7; 19.5 to 33.1) |
| Ischemic heart disease | 24 (6.3; 4.1 to 9.3) | 3 (ANZ) | 14 (6.6; 3.8 to 11.0) | 10 (5.8; 3.0 to 10.8) |
| Pulmonary embolism | 9 (2.3; 1.2 to 4.6) | 3 (ANZ) | 9 (4.2; 2.1 to 8.1) | 0 (0; 0.0 to 2.7) |
| Chronic renal disease | 13 (3.4; 1.9 to 5.9) | 3 (ANZ) | 9 (4.2; 2.1 to 8.1) | 4 (2.3; 0.8 to 6.3) |
| Usual medications, No. (%; 95% CI) | | | | |
| Inhaled beta-sympathomimetics | 289 (74.9; 70.2 to 79.1) | 1 (ANZ) | 167 (77.7; 71.4 to 82.9) | 122 (71.3; 63.9 to 77.9) |
| Inhaled anticholinergics | 49 (12.7; 9.7 to 16.6) | 2 (ANZ) | 35 (16.4; 11.8 to 22.2) | 14 (8.2; 4.7 to 13.6) |
| Inhaled corticosteroids | 177 (46.0; 40.9 to 51.1) | 2 (ANZ) | 112 (52.3; 45.4 to 59.2) | 65 (38.0; 30.8 to 45.8) |
| Oral corticosteroids | 52 (13.5; 10.4 to 17.5) | 3 (ANZ) | 37 (17.4; 12.7 to 23.3) | 15 (8.8; 5.2 to 14.3) |
| Leukotriene receptor antagonists | 18 (4.7; 2.9 to 7.5) | 3 (ANZ) | 8 (3.8; 1.8 to 7.5) | 10 (5.8; 3.0 to 10.8) |
| Methylxanthines | 11 (2.9; 1.5 to 5.2) | 3 (ANZ) | 3 (1.4; 0.4 to 4.4) | 8 (4.7; 2.2 to 9.3) |
| Home oxygen | 4 (1.0; 0.3 to 2.8) | 3 (ANZ) | 3 (1.4; 0.4 to 4.4) | 1 (0.6; 0.0 to 3.7) |
| Arrival by ambulance, No. (%; 95% CI) | 115 (30.4; 25.9 to 35.4) | 9 (4 ANZ, 5 SEA) | 79 (37.3; 30.8 to 44.2) | 36 (21.7; 15.8 to 28.9) |

IQR, interquartile range; ANZ, Australia and New Zealand; SEA, South East Asia and Hong Kong

Table 2. Clinical Features and Investigations

| Variable | Result (N=387) | Missing data |
|---|---|---|
| Duration of symptoms (days), median (IQR) | 2 (1-4) | 8 |
| Ability to speak, No. (%; 95% CI) | | 72 |
| Unable | 12 (3.8; 2.1 to 6.7) | |
| Phrases | 47 (14.9; 11.3 to 19.5) | |
| Sentences | 118 (37.5; 32.1 to 43.1) | |
| Normal | 138 (43.8; 38.3 to 49.5) | |
| Pulse rate (beats per minute), median (IQR) | 99 (86-110) | 7 |
| Pulse rate ≥ 120, No. (%; 95% CI) | 53 (13.9; 10.7 to 17.9) | |
| Respiratory rate (breaths per minute), median (IQR) | 22 (20-25) | 11 |
| Respiratory rate ≥ 30, No. (%; 95% CI) | 41 (10.9; 8.0 to 14.6) | |
| Systolic blood pressure (mmHg), median (IQR) | 133 (120-147) | 13 |
| Systolic blood pressure < 100mmHg, No. (%) | 10 (2.7; 1.4 to 5.0) | |
| Temperature < 35$^{o}$C or ≥ 38.5$^{o}$C, No. (%; 95% CI) | 21 (5.6; 3.6 to 8.6) | 13 |
| Oxygen saturation on room air (%), No. (%; 95% CI) | | 40[a] |
| <94% | 59 (17.0; 13.3 to 21.5) | |
| <90% | 21 (6.1; 3.9 to 9.3) | |
| Findings on auscultation, No. (%; 95% CI) | | 9 |
| Wheeze | 216 (57.1; 52.0 to 61.2) | |
| Widespread rhonchi | 72 (19.1; 15.3 to 23.5) | |
| Normal | 63 (16.7; 13.1 to 20.9) | |
| Local rhonchi/ bronchial breathing | 16 (4.2; 2.5 to 6.9) | |
| Basal rales | 9 (2.4; 1.2 to 4.6) | |
| Widespread rales | 2 (0.5; 0.1 to 2.1) | |
| White cell count > 15.0 x $10^{9}$/L, No. (%; 95% CI) | 31 (13.3; 9.4 to 18.5) | 154 |
| Blood gas taken (venous or arterial), No. (%; 95% CI) | 91 (23.5; 19.34 to 28.1) | 0 |

| | | |
|---|---|---|
| $pCO_2$ > 50mmHg | 4 (1.0; 0.3 to 2.8) | |
| pH < 7.3 | 8 (2.1; 1.0 to 4.2) | |
| Imaging, No. (%; 95% CI) | | 1 |
| Chest X-ray | 272 (70.5; 65.6 to 74.9) | |
| Ventilation perfusion scan or CTPA | 1 (0.3; 0.0 to 1.7) | |
| Lung ultrasound | 1 (0.3; 0.0 to 1.7) | |

CTPA, computed tomography pulmonary angiography

[a] Of these 40 patients, 36 were on supplemental oxygen at initial oxygen saturation reading.

Table 3. Treatment and Outcome

| Variable | Total population (N=387) | Missing data | ANZ (n=216) | SEA (n=171) |
|---|---|---|---|---|
| **Oxygen therapy** | | | | |
| Initial oxygen therapy, No. (%; 95% CI) | | 0 | | |
| None | 274 (70.8; 66.0 to 75.2) | | 153 (70.8; 64.2 to 76.7) | 121 (70.8; 63.2 to 77.3) |
| Face mask | 46 (11.9; 8.9 to 15.6) | | 39 (18.1; 13.3 to 24.0) | 7 (4.1; 1.8 to 8.6) |
| Venturi-type system | 4 (1.0; 0.3 to 2.8) | | 2 (0.9; 0.2 to 3.7) | 2 (1.2; 0.2 to 4.6) |
| Non-rebreather mask | 7 (1.8; 0.8 to 3.9) | | 5 (2.3; 0.9 to 0.6) | 2 (1.2; 0.2 to 4.6) |
| Low flow nasal cannula | 25 (6.5; 4.3 to 9.5) | | 14 (6.5; 3.7 to 10.9) | 11 (6.4; 3.4 to 11.5) |
| Non-invasive ventilation | 1 (0.3; 0.0 to 1.7) | | 1 (0.5; 0.0 to 3.0) | 0 (0.0 to 2.7) |
| Oxygen given but mode unknown | 30 (7.8; 5.4 to 1.1) | | 2 (0.9; 0.2 to 3.7) | 28 (16.4; 11.3 to 23.0) |
| Oxygenation mode used at any time in ED, No. (%; 95% CI) | | 0 | | |
| High-flow nasal cannula | 4 (1.0; 0.3 to 2.8) | | 1 (0.5; 0.0 to 3.0) | 3 (1.8; 0.5 to 5.4) |
| Non-invasive ventilation | 8 (2.1; 1.0 to 4.2) | | 6 (2.8; 1.1 to 6.2) | 2 (1.2; 0.2 to 4.6) |
| Mechanical ventilation | 0 (0; 0.0 to 1.2) | | 0 (0; 0.0 to 2.2) | 0 (0; 0.0 to 2.8) |

| | | | | |
|---|---|---|---|---|
| **Pharmacotherapy, No. (%; 95% CI)** | | | | |
| Inhaled beta sympathomimetic | 339 (87.8; 84.0 to 90.8) | 1 (ANZ) | 183 (85.1; 79.5 to 89.5) | 156 (91.2; 85.7 to 94.8) |
| Inhaled anticholinergic agent | 215 (55.8; 50.7 to 60.9) | 2 (ANZ) | 124 (57.9; 51.0 to 64.6) | 91 (53.2; 45.5 to 60.8) |
| Inhaled bronchodilator (beta-sympathomimetic or anticholinergic) | 340 (87.8; 84.1 to 90.9) | 0 | 184 (85.2; 79.6 to 89.5) | 156 (91.2; 85.7 to 94.8) |
| Oral corticosteroid | 208 (53.9; 48.8 to 58.9) | 1 (ANZ) | 124 (57.7; 50.8 to 64.3) | 84 (49.1; 41.4 to 56.8) |
| Intravenous corticosteroid | 77 (20.1; 16.2 to 24.5) | 3 (ANZ) | 43 (20.2; 15.1 to 26.3) | 34 (19.9; 14.3 to 26.8) |
| Systemic corticosteroid (Oral or IV) | 268 (69.4; 64.5 to 73.9) | 1 (ANZ) | 152 (70.7; 64.1 to 76.6) | 116 (67.8; 60.2 to 74.7) |
| Antibiotic | 89 (23.2; 19.1 to 27.8) | 3 (ANZ) | 65 (30.5; 24.5 to 37.3) | 24 (14.0; 9.4 to 20.4) |
| Both inhaled bronchodilators and systemic corticosteroids | 258 (66.8; 61.9 to 71.5) | 1 (ANZ) | 144 (67.0; 60.2 to 73.1) | 114 (66.7; 59.0 to 73.6) |
| **Outcome** | | | | |
| Disposition, No. (%; 95% CI) | | 0 | | |
| Home (including via an ED observation unit) | 253 (65.4; 60.4 to 70.1) | | 130 (60.2; 53.3 to 66.7) | 123 (71.9; 64.8 to 78.1) |
| Inpatient ward (excluding ICU) | 122 (31.5; 27.0 to 36.4) | | 76 (35.2; 28.9 to 42.0) | 46 (26.9; 20.6 to 34.3) |

| | | | | |
|---|---|---|---|---|
| ICU | 11 (2.8; 1.5 to 5.2) | | 9 (4.2; 2.1 to 8.0) | 2 (1.2; 0.2 to 4.6) |
| Transfer | 1 (0.3; 0.0 to 1.7) | | 1 (0.5; 0.0 to 3.0) | 0 (0; 0.0 to 2.7) |
| Death in ED | 0 (0; 0.0 to 1.2) | | 0 (0; 0.0 to 2.2) | 0 (0; 0.0 to 2.7) |
| In-hospital mortality | 0 (0; 0.0 to 1.2) | | 0 (0; 0.0 to 2.2) | 0 (0; 0.0 to 2.7) |
| Length of stay for admitted patients (days), median (IQR) | 4 (3-6) | 1 (SEA) | 4 (3-5) | 4 (3-6) |

IQR, interquartile range; ANZ, Australia and New Zealand; SEA, South East Asia and Hong Kong